

REMARKS/ARGUMENTS

Claims 1-31 are pending in the subject application. Claims 1-31 presently stand rejected. Claims 1-2, 4, 8, and 19-31 have been amended by the present amendment. Claims 5-7 and 16 have been canceled without prejudice to or disclaimer of the subject matter encompassed thereby. No new matter is added by way of claim amendment. Therefore, upon entry of the present amendment, claims 1-4, 8-15, and 17-31 will remain pending in the subject application. Reexamination and reconsideration of the claims are respectfully requested in view of these amendments and the following remarks. The Examiner's comments in the Office Action are addressed below in the order set forth therein.

The Rejection of Claims 1-31 Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claims 1-31 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Office Action acknowledges that the specification is enabled for a limited number of nucleotides linked through a terminal phosphate group to a solid support and the synthesis thereof. The Office Action asserts, however, that the specification does not reasonably provide enablement for the vast array of compounds, some linked to a solid support and some not linked to a solid support, and the synthesis thereof, encompassed by instant claims 1-30, and to the method of testing encompassed by claim 31.

Applicants have amended claims 1, 28, and 31 by deleting therefrom the terms "tag" and/or "protective group," and deleting from claim 1 embodiments wherein $X = 0$. Applicants also have canceled claim 16, which depends from claim 1 and further defines the term "tag." Accordingly, Applicants respectfully submit that the claims as currently amended are directed to embodiments of compositions of Formula I wherein $x = 1$ and the variable "Y" is "a solid support." Applicants further submit that embodiments of Formula I wherein Y is a solid support and their synthesis are enabled by the numerous examples disclosed in the application as filed.

The Office Action further asserts on page 3, that "[t]he instant disclosure provides a large number of examples of how to make compounds usable in affinity chromatography, but only one prospective description, and no specific embodiments, describing how these compounds might

be applied to actual affinity chromatographies.” Office Action, page 3, paragraph F. The Office Action also asserts that “there are many synthetic working examples, but no working examples of how any one of the instant disclosed compounds may be used to carry out affinity chromatography.” Office Action, page 3, paragraph G.

Applicants note that “[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” Manual of Patent Examining Procedure (hereinafter “MPEP”) § 2164.01 (quoting *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988) (emphasis added)). Applicants respectfully submit that the use of γ -phosphate-linked ATP affinity columns for purifying, for example, a protein kinase, see, e.g., U.S. Patent No. 5,536,822 to Haystead (hereinafter “the ‘822 patent”), and for screening diverse arrays of materials for bioactive compounds, see, e.g., PCT International Patent Application Publication No. WO 00/63694 to Haystead, each of which is incorporated by reference in the subject application, is known in the art. Accordingly, one of ordinary skill in the art upon review of the instant disclosure and what is known in the art, could use the presently disclosed nucleotide affinity medium of Formula I for screening a test compound as disclosed in claim 31 as currently amended.

Further, similar to *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988), where the Court of Appeals for the Federal Circuit (hereinafter “the CAFC”) reversed the Patent Office’s determination that the claims at issue did not satisfy the enablement requirement, Applicants respectfully submit that the subject application provides “considerable direction and guidance” in the specification; there was “a high level of skill in the art at the time the application was filed;” and “all of the methods needed to practice the invention were well known.” MPEP § 2164.01(a) (quoting *In re Wands*, 858 F.2d at 740, 8 U.S.P.Q.2d at 1046 and noting that the court concluded that “it would not require undue experimentation ... to practice the claimed invention”).

It further appears that the Office Action is requiring Applicants to provide working examples of how the claimed compositions can be applied to actual affinity chromatography. Applicants note that “[c]ompliance with the enablement requirement ... does not turn on whether

an example is disclosed.” MPEP § 2164.02. Further, “[a]n applicant need not have actually reduced the invention to practice prior to filing.” *Id.* (discussing *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 U.S.P.Q.2d 1302, 1304 (Fed. Cir. 1987)). Additionally, “[t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *Id.* (citing *In re Borkowski*, 422, F.2d 904, 908, 164, U.S.P.Q. 642, 645 (C.C.P.A. 1970)). Finally, “if all of the other factors point toward enablement, then the absence of working examples will not by itself render the invention non-enabled.” *Id.* (noting that a “lack of working examples ... should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement”).

Applicants respectfully submit that the specification as originally filed enables one of ordinary skill in the art to make or use the subject matter commensurate in scope with the claims as currently amended without undue experimentation. For example, as provided in the Rule 37 C.F.R. § 1.132 Declaration of Dr. Steven E. Hall, which is attached herewith as **Exhibit A**, Applicants demonstrate the use of an affinity ligand bound to a solid support, prepared as described in Example 45 of the application as filed, to screen for drug candidates.

Accordingly, in view of the above Amendment and Remarks, and the experimental data presented in the Rule 37 C.F.R. § 1.132 Declaration of Dr. Steven E. Hall, Applicants respectfully request that the rejection of claims 1-31 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, be withdrawn at this time. Applicants respectfully submit that claims 1-31 as currently amended are in condition for allowance and respectfully request the same.

The Objection of Claims 19, 20, 29 and 30 Should Be Withdrawn

Claim 19 and claim 20 have been objected to as lacking proper terminal punctuation. Applicants have amended claim 19 and claim 20 to have the proper terminal punctuation.

Claim 29 and claim 30 have been objected to as lacking proper terminal punctuation and also lacking the term “and” between the last two Markush group members. Applicants have amended claim 29 and claim 30 to have the proper terminal punctuation and have inserted the term “and” between the last two Markush group members.

Applicants respectfully submit that the objections to claims 19, 20, 29, and 30 have been addressed. Applicants further submit that claims 19, 20, 29, and 30 as currently amended are in condition for allowance and respectfully request the same.

The Rejection of Claims 1-6, 8, 16-28, and 31 Under 35 U.S.C. § 112,

Second Paragraph Should Be Withdrawn

Claim 1-6, 8, 16-28 and 31 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for the following reasons, which are addressed in the order as they are presented in the Office Action.

The Office Action asserts that in claim 1, line 1, and also in claims 2-8 and 16-27, the term “composition” is technically erroneous because the term allegedly implies the presence of two or more separate substances. The Examiner suggests that the term “compound” should be substituted for the term “composition.” Applicants note that “[t]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention.” MPEP § 2111.01 (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313, 75 U.S.P.Q.2d 1321, 1326 (Fed. Cir. 2005) (*en banc*)). Applicants note that the ordinary meaning of the term “composition” is “[t]he combining of distinct parts or elements to form a whole.” *The American Heritage College Dictionary*, 3rd ed., Houghton Mifflin Company, Boston (1993), p. 286, which attached herewith as **Exhibit B**. In the subject application the term “composition” as recited in the claims as currently amended refers to the combination of a solid support, an alkylamine linker, and a 5'-nucleosidyl group or a non-naturally occurring 5'-nucleosidyl group. Thus, the presently claimed composition of Formula I arises from “the combining of distinct parts ... to form a whole.” In contrast, one of ordinary skill in the art would recognize the term “compound” to mean “[a] substance composed of atoms or ions of two or more elements in chemical combination” wherein “[t]he constituents are united by bonds or valence forces.” *Hawley's Condensed Chemical Dictionary*, 14th ed., John Wiley & Sons, Inc., New York (2001), p. 289, which attached herewith as **Exhibit C**. A “compound” is further defined as “a homogenous entity where the elements have definite proportions by weight and are represented by a chemical formula.” *Id.* Applicants respectfully submit that it is not

appropriate to characterize the structure of Formula I as a “compound” because the structure represented by Formula I includes attaching a nucleosidyl group through a linker to a solid support. Thus, Applicants respectfully submit that the structure represented by Formula I can best be described as a “composition” as that term would be recognized by one of ordinary skill in the art.

The Office Action asserts that in claim 1, line 1, the term “comprising” is incorrect because the term allegedly implies that the chemical structure of the compound being claimed contains additional structural component(s) not defined in the claim. Applicants have amended claims 1, 23-28, and 31 by deleting the term “comprising” and inserting the transitional phrase “consisting essentially of.” Applicants note that the use of “the transitional phrase ‘consisting essentially of’ limits the scope of the claim to the specified materials ‘and those that do not materially affect the basic and novel characteristic(s)’ of the claimed invention.” MPEP § 2111.03 (quoting *In re Herz*, 537 F.2d 549, 551-52, 190 U.S.P.Q. 461, 463 (C.C.P.A. 1976)). Thus, Applicants respectfully submit that the transitional phrase “consisting essentially of” is appropriate for use in claims 1, 8, 23-28, and 31, which recite compositions of general formulae I-VI.

The Office Action suggests that in claim 1, lines 3-4, and in claims 28 and 31, the term “X = 0 or 1” requires that the definitions of R₁ and R₂ be amended to read “when X = 1 R₁ is a covalent bond between Y and R₂, or when X = 0, R₁ is an acyl group, ...” Preliminarily, Applicants note that the variable “X” is limited to the value of “1” in claims 28 and 31 as presently standing. As noted hereinabove, Applicants have amended claim 1 by limiting the value of the variable “X” to “1.” Accordingly, the current amendments render moot the suggestion to distinguish the definition of R₁ when X is 0.

The Office Action asserts that in claim 1, lines 4-10, and in claims 28 and 31, the term “substituted” allegedly renders the claim incompletely defined. Applicants respectfully submit that one of ordinary skill in the art upon review of the instant disclosure and what is known in the art would recognize what is meant by the term “substituted.” Applicants note that the ‘822 patent to Haystead, which is incorporated by reference in the subject application, discloses affinity columns having a linking moiety linked to a solid support, wherein the linking moiety

includes, for example, any straight or branched chain having at least two carbon atoms, which can be substituted with an amine, halogen, nitro, hydroxyl, sulfhydryl, or carboxyl group. See the '822 patent, col. 3, lines 37-57. The '822 patent goes on to list numerous examples of substituted alkyl groups. See the '822 patent, col. 3, lines 57-67, through col. 4, lines 1-6. The '822 patent also discloses substituted phenyl, i.e., aryl groups, for example, phenyl groups substituted with halogen, alkyl, nitro, amine, hydroxyl, sulfhydryl, carboxyl groups, and the like. See the '822 patent, col. 4, lines 9-14. Thus, Applicants respectfully submit that one of ordinary skill in the art would recognize what is meant by the term "substituted" in claims 1, 28, and 31.

The Office Action asserts that in claim 1, lines 8-11, and in claims 28 and 31, the definitions of the variable R_2 is incorrect because it allegedly fails to define the substituent moieties as divalent. The Office Action suggests that the listed substituent groups may be amended to read, for example, "divalent alkyl," etc. Applicants have amended claims 1-3, 8, 28, and 31 by inserting the term "divalent" before each occurrence of the listed substituent groups so that the claims now read, for example, "divalent alkyl," and the like.

The Office Action asserts that in claim 1, line 11, and in claims 28 and 31, the term "K is a heteroatom" allegedly renders the claim incomplete. Applicants have amended claims 1, 8, 28, and 31 by defining the variable "K" to be "NH." Support for this amendment can be found throughout the application as filed, for example, in the numerous examples which include linkers wherein the variable "K" is NH. No new matter has been added by the present amendment.

The Office Action asserts that in claim 1, line 12, and in claims 28 and 31, the term "phosphate group mimic" allegedly renders the claim incompletely defined because the term "phosphate group mimic" is not further defined in the claim. Applicants respectfully submit that the application as filed discloses numerous examples of "phosphate group mimic." For example, see page 12, line 11, through page 14, line 10, of the application as filed. Accordingly, Applicants respectfully submit that one of ordinary skill in the art upon review of the application as filed would recognize what is meant by the term "phosphate group mimic" in claims 1, 28, and 31.

The Office Action assert that in claim 1, line 12, and in claims 28 and 31, the term "nucleoside or nucleoside derivative" is technically incorrect because the substituent groups

being defined allegedly and are not compounds, but are substituent groups. The Office Action suggests that the term be amended to read “a 5'-nucleosidyl group or a 5'-nucleosidyl group wherein the nucleoside is not naturally occurring.” Applicants have amended claims 1, 28, and 31 by deleting the phrase “nucleoside or nucleoside derivative” and inserting the phrase “5'-nucleosidyl group or a 5'-nucleosidyl group wherein the nucleoside is not naturally occurring, or a derivative thereof.”

The Office Action also asserts that the term “derivative” is not further defined, but would be acceptable if a definition of what is meant were asserted into the claim. Applicants respectfully submit that one of ordinary skill in the art upon review of the instant disclosure would appreciate what is meant by the term “derivative” in the claims. For example, on page 15, several references describing the isolation or synthesis of nucleoside derivatives are incorporated by reference. Also, exemplary, non-limiting examples of adenosine derivatives are provided on pages 22-30 of the application as filed. Additional adenosine derivatives are described on page 40, line 30, through page 41, line 6, of the application as filed.

The Office Action asserts that in claim 1, lines 8 and 11, and also in claim 2, 3, 28, and 31, the term “or a combination thereof” renders the claim indefinite because what is meant thereby is not further defined. Applicants respectfully submit that one of ordinary skill in the art upon review of the instant disclosure would recognize what is meant by the term “or a combination thereof.” For example, in Example 37, the variable “R₂” could be characterized as a combination of a non-substituted alkyl group and a heterocycloalkyl group, e.g., piperazine. Likewise, in Example 38, the variable “R₂” could be characterized as a combination of a non-substituted alkyl group and 2,4,8,10-tetraoxaspiro[5.5- undecane]. Further, in Example 73, the variable “R₂” could be characterized as a combination of a non-substituted alkyl group and a non-substituted aryl group, e.g., a phenyl group.

The Office Action asserts that in claim 2, line 1, and claim 3, the term “comprises” is incorrect and is incomplete because claim 2 added subject matter to the definition of variable R₂ that has not been found in claim 1. The Office Action suggests that the term “comprises” should be amended to read “further comprising” to give proper notice of the presence of additional

subject matter. Applicants have amended claims 2 and 3 by inserting the term “further” before the term “comprises” so that the transitional phrase now reads “further comprises.”

The Office Action asserts that in claim 2, line 2, the term “a general formula” implies that there are other alternatives not disclosed in the claim. Applicants have amended claims 2 and 4 by deleting the term “a” and inserting the term “the” to modify the phrase “general formula.”

The Office Action asserts that in claims 5 and 6, line 2, the term “nitrogen atom” renders the claim incompletely defined because the third valence of “N” has not been specified.

Preliminarily, Applicants note that claims 5 and 6 have been canceled by the present Amendment. Applicants further note that the variable “K” has been defined in claims 1, 8, 28, and 31, as “NH,” wherein the hydrogen atom provides the third valence of the nitrogen atom. Support for this amendment can be found through the application as filed, more particularly in the numerous examples, which exemplify embodiments of the presently claimed subject matter in which the variable “K” is defined as “NH.”

The Office Action asserts that claim 8 is improperly dependent because the claim fails to further limit the subject matter from which it depends. Applicants have amended claim 8 to be in independent form, reciting “[a] nucleotide affinity medium comprising an alkyl-linked composition of Formula I,” Support for this amendment can be found in claim 8 as originally filed.

The Office Action asserts that in claim 21, line 5, the term “and” is incorrect because the claim appears to have been drafted with the intent that “ionized variant or a salt thereof” would be alternatives, not additives. The Office Action suggests substitution of the term “or.” Applicants have amended claim 21 as suggested in the Office Action.

The Office Action asserts that in claim 22, and in claims 23-27, the term “adenosine, ... and uridine” are directed to compounds, not substituents. Applicants have amended claims 22-27 by amending the terms “adenosine, guanosine, ...” and the like to read “adenosinyl, guanosinyl, ...” and the like.

The Office Action asserts that the term “analog” in claim 22 is indefinite because there is no further definition of what chemical structures are intended to be included within the scope of the claim. Applicants respectfully submit that one of ordinary skill in the art upon review of the

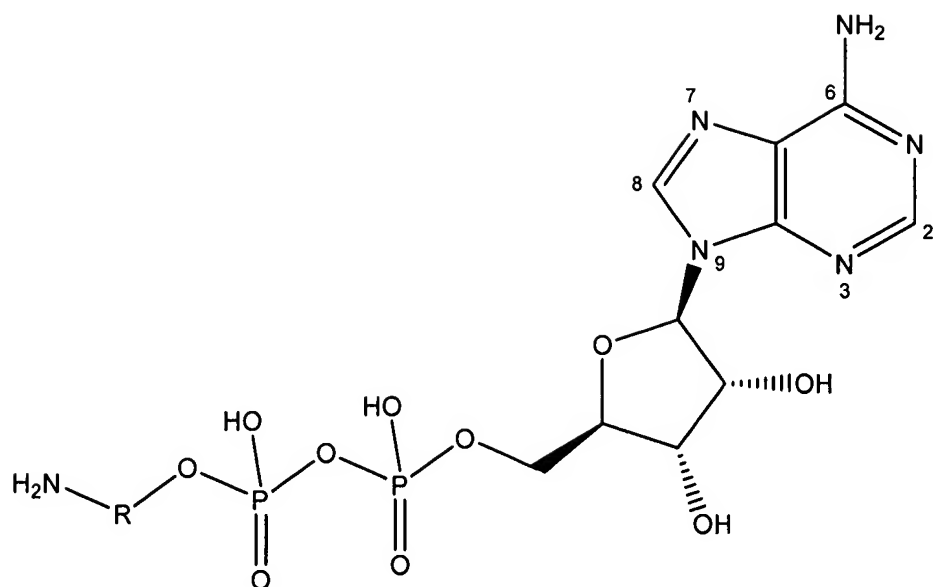
instant disclosure would recognize what is meant by the term “analog.” Applicants note that references describing the isolation or synthesis of nucleoside analogs are incorporated by reference on page 15 of the application as filed. Applicants further note that exemplary, non-limiting examples of γ -alkyl-linked nucleotide analogs of Formulae LII-LV are disclosed on page 33 of the application as filed. Additionally, exemplary ATP analogs are disclosed on pages 37- 39 of the application as filed. Further, non-limiting examples of nucleoside analogs are disclosed on page 40, lines 17-29, of the application as filed.

The Rejection of Claims 1-31 Under 35 U.S.C. § 103(a)
Should Be Withdrawn

Claims 1-31 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Trayer et al. in view of Van Aerschot et al. More particularly, the Office Action asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made, based on the teachings of Trayer et al. to make compounds including the linkers of Van Aerschot et al., which allegedly would read on the instant claimed compounds. Further, the Office Action asserts, based on the teachings of Trayer et al., one of ordinary skill in the art would expect that the resultant compounds would be useful in affinity chromatography.

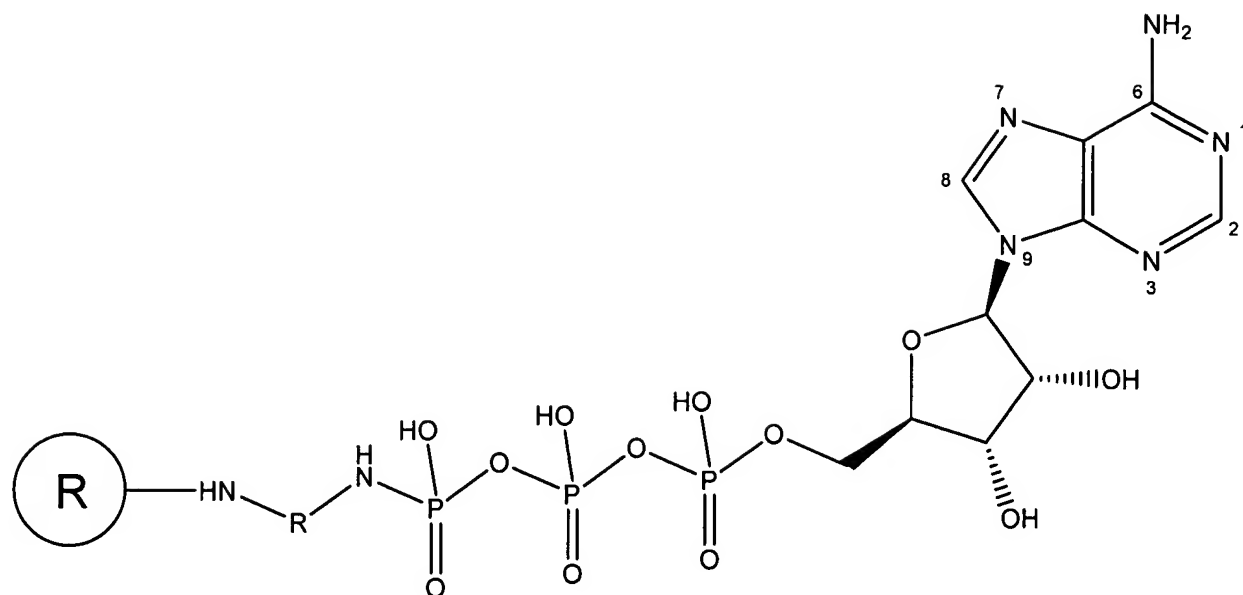
Preliminarily, Applicants note that “[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” MPEP § 2143.03 (citing *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974)). Applicants respectfully submit that neither Trayer et al. and/or Van Aerschot et al., either alone or in combination, teach or suggest all of the claim limitations of the pending claims as currently amended.

Applicants note that Trayer et al. discloses a ligand, for example, compound C in Figure 1, having the following formula:



wherein R is $-(\text{CH}_2)_6-$. Trayer et al. also discloses ligands wherein an alkylamine linker is attached to either position 8 of the purine ring, e.g., Compound A of Figure 1, or position 6 of the purine ring, e.g., Compound B of Figure 1. Applicants further note that ligands disclosed in Trayer et al. having an alkylamine linker attached to, for example, a pyrophosphate group, the linker is attached to the pyrophosphate group through an oxygen atom.

In contrast, the claims of the subject application as currently amended recite ligands having, for example, the following structure:



wherein R is a solid support as disclosed in the instant application.

One of ordinary skill in the art upon review of the presently disclosed subject matter would recognize that the ligands disclosed in Trayer et al. differ from the compositions of the instant claims as presently amended in that the alkylamine linker disclosed in Trayer et al. is attached to a gamma-phosphorous atom of an ADP (or ATP) molecule through an oxygen atom, whereas the linker group of the presently claimed compounds is attached through a nitrogen atom. Thus, Trayer et al., neither alone or in combination with Van Aerschot et al., discloses, teaches, or suggests an alkylamine linker attached to a gamma-phosphorous atom of an ADP (or ATP) molecule through a nitrogen atom.

Applicants respectfully submit that one of ordinary skill in the art would recognize that a linker attached to an oxygen atom is labile, whereas a linker attached to a nitrogen atom is more stable. Further, Applicants respectfully submit that the identity of the polymeric resin, the linker type and length, and ligand density, i.e., the amount of ligand bound per mL of resin, can influence the performance characteristics of ligands bound to a solid substrate for use, for example, in affinity chromatography, e.g., to profile compound libraries for drug discovery.

In sum, Applicants respectfully submit that all of the claim limitations of claims 1-31 are neither taught nor suggested by Trayer et al. and/or Van Aerschot et al., either alone or in combination. Accordingly, Applicants respectfully submit that the Office Action has not

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established a *prima facie* case of obviousness. Accordingly, Applications respectfully request that the rejection of claims 1-31 under 35 U.S.C. § 103(a) over Trayer et al. in view of Van Aerschot et al. be withdrawn at this time.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. § 112, first paragraph; § 112, second paragraph, and § 103(a) are now overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

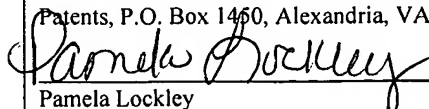


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